

Figure 1A

NOVTRAN cDNA sequence:

atgcagtggtcctgtctggcctgtacctcctcagggtcctccacatgtcctgtctcctctgagagacctgtgcctgtgccacagggaccaagctcttc
cactcctgtatcacctcaacgaacctatgcgcctcctcctggagggtgtgtgtgaagctgcaggcatcacccctggactgtagggtctgagcacccgcc
ctgtccatcatccctgcatgcctctccgttccaggactccttcaacagaccatccctgtcctctcaacaggccccgctctgtctggggaacca
cggacagaggccttccatccccaggcctgaaggccagagtaggtgggaccatcctcgcgaagccggcctcaattctcaaggccatgccgtggagc
cagtgccatctggacctctgggtcaagcaaagggtgtgtgctaatcaaaaggcaggccctcgaggatgccaaaggccccggaatgccagtggaccg
tgaaaaccttctgtgacaaacctgcagtgccttctctgtccagctgtctcctcagctctccatgcatcaagggtggaacagagcaggagcgcagtaatg
cggaaattgacttgcaaagtcgggcccgtcgggattacaattcaaggctgtctgtgaaactcgggcagatccagctgcaaagggcagttccttctcga
gtgcagaacgtgtctggagggttggctcagcccagggtcccaggaaccactgcaagggtggggcgggccctcagagcccttccagagctggg
ggctggtagcccccttggcttggagaaggctcagtacccaacccatccccaggcccagctcggaagggtgtggaactggccccctgtgtcctgtg
gaccagtgtccactgtgcacttcccaggccagccgaacctggcacacactgggtgttccctaaatagccatggagggtattgtggcatggagagctgtc
gattccagaaacctcctggacatagggtgggagctcatctgcagaagctgcctga

Figure 1B

NOVTRAN Protein Sequence:

MQWSCLACTLLRVLPHVLSLLRDPVPVPTGTKLFHSCITSTNPCASFLEVAVEAAGITPW
TVGSEHPPCPYPSSLHASPFDTDSFNRPSPAPLNRPRSAGEPRTEAFPSPGLKARVGGTILAE
AGLNSQGHAVEPVPSGPSGSSKGCVLIKGRPSRMPKARECPVDRENLLL TNPAVPSLLQL
LSSSPCIKVETEQUERSNAEFDLQSRARDYNSRLLLKLQIPAAKGSSFLELQNVSGGVG
SARGPRNHCKVGAGPQSPFPELGAGSPPLALEKVSTQPIQARLRKGVDWPPVSPGDQC
PLCTLPGQPNLAHTGCSLNSHGGYCGMESCRFQKPPGHRAGSSSAEAA

Figure 2A

BlastN for NOVTRAN:

gb:GENBANK-ID:H55724|acc:H55724 CHR220663 Chromosome 22 exon Homo sapiens
genomic clone C22_916 5', mRNA sequence - Homo sapiens, 171 bp.

Minus Strand HSPs:

Score = 585 (87.8 bits), Expect = 1.0e-19, P = 1.0e-19

Identities = 117/117 (100%), Positives = 117/117 (100%), Strand = Minus /
Plus.

Query: 735 ACCTCGGGCTGAGCCAACCCCTCCAGACACGTTCTGCAGCTCGAGGAAGGAACTGCCCTT 676

Sbjct: 18 ACCTCGGGCTGAGCCAACCCCTCCAGACACGTTCTGCAGCTCGAGGAAGGAACTGCCCTT 77

Query: 675 TGCAGCTGGGATCTGCCCCGAGTTTCAGCAGCAGCCTTGAATTGTAATCCCGAGCGGC 619

Sbjct: 78 TGCAGCTGGGATCTGCCCCGAGTTTCAGCAGCAGCCTTGAATTGTAATCCCGAGCGGC 134

Figure 2B

BlastX for NOVTRAN:

No Hits:

ptnr:SWISSPROT-ACC:P22357 ANOTHER-SPECIFIC PROTEIN SF18...	-3	102	0.0093	1
ptnr:SPTREMBL-ACC:Q26876 PROTECTIVE RECOMBINANT ANTIGE...	-3	87	0.018	1
ptnr:TREMBLNEW-ACC:AAD41775 PRO-ALPHA-2(I) COLLAGEN - ...	-3	86	0.061	2
ptnr:PIR-ID:S46272 anther-specific protein - common su...	-3	94	0.073	1
ptnr:SPTREMBL-ACC:Q26874 PROTECTIVE RECOMBINANT ANTIGE...	-3	78	0.16	1
ptnr:SPTREMBL-ACC:Q92029 ALPHA-1 COLLAGEN TYPE III - G...	-3	86	0.19	3
ptnr:SWISSPROT-ACC:P46804 SPIDROIN 2 (DRAGLINE SILK FI...	-3	101	0.24	1
ptnr:SPTREMBL-ACC:O57808 103AA LONG HYPOTHETICAL PROTE...	+2	76	0.25	1
ptnr:SWISSNEW-ACC:P41484 PROLINE-RICH ANTIGEN (36 KD A...	-3	95	0.26	1

CuraBLASTX Analysis of AC007663_A

PUBLIC DATABASE

Query= AC007663_A Cura_109 transmembrane protein
(1047 letters)

Database: /opt/database/public/blast/protnr
577,633 sequences; 178,813,065 total letters.

		Reading	High	Smallest	
		Frame	Score	Sum	
Sequences producing High-scoring Segment Pairs:				Probability	
				P(N)	N
ptnr:SWISSPROT-ACC:P22357 ANOTHER-SPECIFIC PROTEIN SF18...	-3	102	0.015	1	
ptnr:pir-id:S12246 anther-specific protein SF18 precur...	-3	102	0.015	1	

PATENT DATABASE

CuraBLASTX Analysis of AC007663_A

Query= AC007663_A Cura_109 transmembrane protein
(1047 letters) of query sequence in all 6 reading frames

Database: /opt/database/licensed/blast/geneseq_aa
349,121 sequences; 51,277,408 total letters.

		Reading	High	Smallest	
		Frame	Score	Sum	
Sequences producing High-scoring Segment Pairs:				Probability	
				P(N)	N
patp:R28916 Type III procollagen (prior art) - Homo sa...	+1	81	0.059	3	
patp:W03454 Mutant mouse c-AKT non-translation region ...	+1	81	0.075	1	
patp:G04146 Arabidopsis thaliana protein fragment SEQ ...	-3	80	0.095	1	

Figure 3A

NOVNEUR cDNA sequence:

Regions 135319 to 135129 (1-190bp) and 134487 to 134314 (191 to 364bp) of the genomic clone (in - frame). Further extended using ESTs AI739078, AI767488, and AI796217.

AGCGCGCCCGAACGAAGCCGCGGCCCGGGCACAGCATGGCCCGCGGGAGGGCGCTCGGATGTTCCGGC
AGCCTCCTGCACTTCGCCCTGCTCGCTGCCGGCGTCGTCCCGCTCAGCTGGGATCTCCCGGAGCCCCGCA
GCCGAGCCAGCAAGATCCGAGTGCCTCGCGAGGCAAGCTCTGGGCCATCGGTTCATTCATGGGCAAGAA
GAGTCTGGAGCCTTCCAGCCCATTCCCATTTGGGGACAGCTCCCCACAGCTCCCTGAGGGACCAGCGACTG
CAGCTGAGTCATGATCTGCTCGGAATCCTCCTGCTAAAGAAGGCTCTGGGCGTGAGCCTCAGCCGCCCCG
CACCCCAAATCCAGTACAGGAGGCTGCTGGTACAAATACTGCAGAAATGACACCAATAATGGGGCAGACA
CAACAGCGTGGCTTAGATTGTGCCCCACCCAGGGAAGGTGCTGAATGGGACCCGTGTTGATGGCCCCATCTG
GATGTAAATCCTGAGCTCAAATCTCTGTTACTCCATTACTGTGATTTCTGGCTGGGTCAACCAGAAATATC
GCTGATGCAGACACAGATTATGTTCCCTGCTGTATTTCCCTGCTTCCCTGTTGAATTGGTGAATAAAACCTT
GCTCTATACATACAAA

Figure 3B

NOVNEUR Protein sequence:

MFGSLHLHFALLAAGVVPLSWDLPEPRSRASKIRVHSRGKLWAIGHFMGKKSLEPSSPSPLGTAPHTSLRDQRLQLSH
DLLGILLKKALGVSLSRPAPQIQYRLLVQILQK

Figure 4A

BlastN for NOVNEUR:

gb:GENBANK-ID:HUMNKB|acc:M21551 Human neuromedin B mRNA, complete cds -
Homo sapiens, 640 bp (RNA).

Top Previous Match Next Match
Length = 640

Plus Strand HSPs:

Score = 3055 (458.4 bits), Expect = 9.1e-132, P = 9.1e-132

Identities = 629/639 (98%), Positives = 629/639 (98%), Strand = Plus / Plus

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Query:      2 GCGCGCCCGAACGAAGCCGCGGCCCGGGCACAGC-ATGGCCCG-CGG-CGGGAGGGCGCT 58
             GCGCGCCCGAACGAAGCCGCGGCCCGGGCACAGC ATGGCCCG CGG CGG GGGCGCT
Sbjct:      2 GCGCGCCCGAACGAAGCCGCGGCCCGGGCACAGCCATGGCCCGCGGGCGGG-GGGCGCT 60

Query:     59 CGGATGTTTCGGCAGCCTCCTGCAC'TTCGCCCTGCTCGCTGCCGGCGTCTGTCCTCCGCTCAGC 118
             CGGATGTTTCGGCAGCCTCCTGC C'TTCGCCCTGCTCGCTGCCGGCGTCTG CCGCTCAGC
Sbjct:     61 CGGATGTTTCGGCAGCCTCCTGCTC'TTCGCCCTGCTCGCTGCCGGCGTCTGCCCGCTCAGC 120

Query:    119 TGGGATCTCCCGGAGCCCCGAGCCGAGCCAGCAAGATCCGAGTGCAC'TCGCGAGGCAAG 178
             TGGGATCTCCCGGAGCCCCGAGCCGAGCCAGCAAGATCCGAGTGCAC'TCGCGAGGCAA
Sbjct:    121 TGGGATCTCCCGGAGCCCCGAGCCGAGCCAGCAAGATCCGAGTGCAC'TCGCGAGGCAAC 180

Query:    179 CTCTGGGGCCATCGGTCACT'TCATGGGCAAGAAGAGTCTGGAGCCT'TCCAGCCCATCCCCA 238
             CTCTGGGGCA CGGTCACT'TCATGGGCAAGAAGAGTCTGGAGCCT'TCCAGCCCATCCC A
Sbjct:    181 CTCTGGGGCCACCGGTCACT'TCATGGGCAAGAAGAGTCTGGAGCCT'TCCAGCCCATCCC-A 239

Query:    239 TTGGGGACAGCTCCCCACACCTCCC-TGAGGGACCAGCGACTGCAGCTGAGTCATGATCT 297
             TTGGGGACAGCTCCCCACACCTCCC TGAGGGACCAGCGACTGCAGCTGAGTCATGATCT
Sbjct:    240 TTGGGGACAGCTCCCCACACCTCCCCTGAGGGACCAGCGACTGCAGCTGAGTCATGATCT 299

Query:    298 GCTCGGAATCCTCCTGCTAAAGAAGGCTCTGGGCGTGAGCCTCAGCCGCCCCCGCACCCCA 357
             GCTCGGAATCCTCCTGCTAAAGAAGGCTCTGGGCGTGAGCCTCAGCCGCCCCCGCACCCCA
Sbjct:    300 GCTCGGAATCCTCCTGCTAAAGAAGGCTCTGGGCGTGAGCCTCAGCCGCCCCCGCACCCCA 359

Query:    358 AATCCAGTACAGGAGGCTGCTGGTACAAATACTGCAGAAATGACACCAATAAT-GGGGCA 416
             AATCCAGTACAGGAGGCTGCTGGTACAAATACTGCAGAAATGACACCAATAAT GGGGCA
Sbjct:    360 AATCCAGTACAGGAGGCTGCTGGTACAAATACTGCAGAAATGACACCAATAATAGGGGCA 419

Query:    417 GACACAACAGCGTGGCTTAGATTGTGCCACCCAGGGAAGGTGCTGAATGGGACCCTGTT 476
             GACACAACAGCGTGGCTTAGATTGTGCCACCCAGGGAAGGTGCTGAATGGGACCCTGTT
Sbjct:    420 GACACAACAGCGTGGCTTAGATTGTGCCACCCAGGGAAGGTGCTGAATGGGACCCTGTT 479

Query:    477 GATGGCCCCATCTGGATGTAAATCCTGAGCTCAAATCTCTGTTACTCCATTACTGTGATT 536
             GATGGCCCCATCTGGATGTAAATCCTGAGCTCAAATCTCTGTTACTCCATTACTGTGATT
Sbjct:    480 GATGGCCCCATCTGGATGTAAATCCTGAGCTCAAATCTCTGTTACTCCATTACTGTGATT 539

Query:    537 TCTGGCTGGGTCAACAGAAATATCGCTGATGCAGACACAGATTATGTTTCCTGCTGTATTT 596
             TCTGGCTGGGTCAACAGAAATATCGCTGATGCAGACACAGATTATGTTTCCTGCTGTATTT
Sbjct:    540 TCTGGCTGGGTCAACAGAAATATCGCTGATGCAGACACAGATTATGTTTCCTGCTGTATTT 599

Query:    597 CCTGCTTCCCTGTTGAATTGGTGAATAAAACCTTGCTCTAT 637
             CCTGCTTCCCTGTTGAATTGGTGAATAAAACCTTGCTCT T
Sbjct:    600 CCTGCTTCCCTGTTGAATTGGTGAATAAAACCTTGCTCTTT 640

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Figure 4B

BlastX for NOVNEUR:

ptnr:SWISSPROT-ACC:P08949 NEUROMEDIN B-32 PRECURSOR [CONTAINS: NEUROMEDIN B] - Homo sapiens (Human), 121 aa.

Top Previous Match Next Match

Length = 121

Plus Strand HSPs:

Score = 513 (180.6 bits), Expect = 1.9e-48, P = 1.9e-48

Identities = 105/118 (88%), Positives = 105/118 (88%), Frame = +2

Query: 44 RREGARMFGSLLHFALLAAGVVPLSWDLPEPRSRASKIRVHSRGKLWAIGHFMGKKSLEP 223

R GARMFGSLL FALLAAGV PLSWDLPEPRSRASKIRVHSRG LWA GHFMGKKSLEP

Sbjct: 4 RAGGARMFGSLLLFALLAAGVAPLSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKSLEP 63

Query: 224 SSPSPGLGTAPHTSLRDQRLQLSHDLLGILLKKALGVSLSRPAPQIQYRRLVQILQK 397

SSPS G P LRDQRLQLSHDLLGILLKKALGVSLSRPAPQIQYRRLVQILQK

Sbjct: 64 SSPSHWGQLPTPPLRDQRLQLSHDLLGILLKKALGVSLSRPAPQIQYRRLVQILQK 121

Figure 5

ClustalW for NOVNEUR:

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (i.e., regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (e.g., L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

Sequences used:

- 1) A37178 (neuromedin B precursor + rat): Locus A37178, accession A37178, PID - g112182
- 2) NEUB_HUMAN (NEUROMEDIN B-32 PRECURSOR): Locus - NEUB_HUMAN, accession - P08949, PID - g1346684

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Neuromedin_New_REVCOMP  -----MFGSLLHFAALLAAGVPLSWDLPEPRSRASKIRVHSRGKLWALGHFMGKKS
A37178                  MTRQAGSTWLLRGLLLFALEVSGITPFSWDLPEPRSRASKIRVHPRGNLWATGHFMGKKS
NEUB_HUMAN              MARRAGGARMFGSLLLFALLAAGVPLSWDLPEPRSRASKIRVHSRGNLWATGHFMGKKS

Neuromedin_New_REVCOMP  LEPSSPSPLGTAPHTSLRDQRLQLSHDLLGILLKKALGVSLSRPAPQIQYRRLVQIL●
A37178                  LEPPSLSLVGTAPPITQREQRLQLSHDLLRIILLQKALGMNLSGPAPPIQYRRLLOK---
NEUB_HUMAN              LEPSSPSHWGQLPTPLRDQRLQLSHDLLGILLKKALGVSLSRPAPQIQYRRLV●ILQ

Neuromedin_New_REVCOMP  K
A37178                  -
NEUB_HUMAN              K
```

Figure 6A

NOVGON cDNA sequence:

1
ATGAAGCTGGCATTCTCTTCCTTGGCCCCATGGCCCTCCTCCTTCTGGCTGGCTATGGCTGTGTCTCGGTGCCTCCAG
81
TGGGAACCTGCGCACCTTTGTGGGCTGTGCCGTGAGGGAGTTTACTTTCCTGGCCAAGAAGCCAGGCTGCAGGGGCCTTC
161
GGATCACCAAGGATGCCTGCTGGGGTCGCTGTGAGACCTGGGAGAAAACCCATTCTGGAACCCCTATATTGAAGCCCAT
241
CATCGAGTCTGTACCTACAACGAGACCAAACAGGTGACTGTCAAGCTGCCCAACTGTGCCCCGGGAGTCGACCCCTTCTA
321
CACCTATCCCGTGGCCATCCGCTGTGACTGCGGAGCCTGCTCCACTGCCACCAAGGAGCTGAGGTTGATGCCAGGGGAAG
401
CTGCTGTGGCACTGGGCTTCTGGTGTGAGCGTAGGAGACAGGGATCTAGGACAACAGGGACCAGGTGGCGACATGCAGCT
481
GTAAGAGACAAGGTGAGTCTCCTGAAGGCAGTAGATGGTTGGAATGGGCTGCTTGGGGACCCAGCGAGCTCCCAGGGCCT
561
TTCTGCTTCTTCCTGTACCCCTGTATTTCCCTTGGCTTTCCAAATTGACTCAGCTTCTGGTAAAGTTGGAACTTTTCCA
641
GCAAACAGACCTTCATCTTCTCCAGTGCAGAGATTACATTAGGAGGAACATGA

Figure 6B

NOVGON Protein Sequence:

MKLAFLFLGPMALLLLAGYGCVLGASSGNLRTFVGCAVREFTFLAKKPGCRGLRITTD
CWGRCEWKEPPYIEAHHRVCTYNETHQVTVKLPNCAPGVDPFYTYTPVAIRCDG
ACSTATTELRLMPGEAAVALGFWCQRRRQGSRTTGTRWRHAAVRDKVSLLKAVD
GW
NLLGDPASSQGLSASSCTPVFPLAFQIDSASGKVGNFSSKQTFIFSSAEITLGGT*

Figure 7A

BlastN for NOVGON:

AF146151 Salmo salar gonadotropin II beta subunit mRNA,
partial cds - Salmo salar, 266 bp (RNA).

Top Previous Match Next Match
Length = 266

Plus Strand HSPs:

Score = 208 (31.2 bits), Expect = 0.043, P = 0.042

Identities = 124/205 (60%), Positives = 124/205 (60%), Strand = Plus / Plus

Query: 177 CTGCTGGGGTCGCTGTGAGACCTGGGAGAAACCCATTCTGGAACCCCCCTATATTGAAGC 236
CTGC G GG C CTG G ACC GGAG CC TT T AA CCC AT TT A C
Sbjct: 34 CTGCAGTGGCCACTGCGTCACCAAGGAG---CCGGTTTTTC-AAGAGCCC-ATTTTCCACC 88

Query: 237 CCAT-C-ATCGAGTCTGTACCTACAACGA-GACCAAACAGGTGACTGTCAAGCTGCCCCAA 293
T C A C GT TG ACCTAC GA G CC A G AC TC CT CC A
Sbjct: 89 GTGTACCAGCATGTGTGCACCTACCGGGACGTCCGCT-ATGAAACGATCCGCCTACCTGA 147

Query: 294 CTGTGCCCCGGGAGTGGACCC-CTTCTACACCTATCCCGTGGCCATCCGCTGTGACTGCG 352
CTGT CCCC G GT GACC C T T CACCTA CC GTGGC T GCTGTGACTGC
Sbjct: 148 CTGTCCCCCTTGGGTGGACCATCATGT-CACCTACCCTGTGGCTCTGAGCTGTGACTGCA 206

Query: 353 GAGCCTGCTCCACTGCCACCACGGAGCTG 381
G CTG CA G CAC C GA CTG
Sbjct: 207 GCCTCTGTAACATGGACACTTCTGA-CTG 234

Figure 7B

BlastX for NOVGON:

P01235 GONADOTROPIN BETA CHAIN PRECURSOR - *Cyprinus carpio* (Common carp), 144 aa.

Score = 203 (71.5 bits), Expect = 2.3e-16, P = 2.3e-16
Identities = 37/85 (43%), Positives = 52/85 (61%)

Query: 42 TFLAKKPGC-RGLRITTDACWGRCEWKEPILEPPYIEAHHRVCTYNETKQVTVKLPNCA 100
T +K GC + L + T C G C T E P+ + P+ + VCTY + + TV+LP+C
Sbjct: 39 TVAVEKEGCPKCLVLQTTICSGHCLTKE-PVYKSPFSTVYQHVCITYRDVRYETVRLPDCP 97

Query: 101 PGVDPFYTYTPVAIRCDGACSTATTE 126
PGVDP TYPVA+ CDC C+ T++
Sbjct: 98 PGVDPHITYPVALSCDCSLCTMDTSD 123

>ptnr:SWISSNEW-ACC:Q9YGH2 GONADOTROPIN BETA-II CHAIN PRECURSOR (GTH-II-BETA)
- *Clupea pallasii* (Pacific herring), 149 aa.

Plus Strand HSPs:

Score = 206 (72.5 bits), Expect = 1.0e-15, P = 1.0e-15
Identities = 47/117 (40%), Positives = 63/117 (53%), Frame = +1

Query: 28 PMALLLLAGYGCVLG--ASSGNLRTFVGCAVREFTFLAKKPGC-RGLRITTDACWGRCE 198
P, +LL CVL A NL+ C + T +K GC R L T C G C T
Sbjct: 5 PECTILLLLCMCVLAVPAQCFNLQP---CVLVNETVSVEKEGCPRLVFRITICSGHCPT 61

Query: 199 WEKPILEPPYIEAHHRVCTYNETKQVTVKLPNCAPGVDPFYTYTPVAIRCDGACSTATTE 378
E P+ + P+ + VCTY + T++LP+CA GVDP TYPVA+ C+C CS T++
Sbjct: 62 KE-PVYKSPFSVQNQHVCITYGNFRYETIRLPDCADGVDPVLTYPVALSCECSLCSMDTSD 120

>patp:R15106 hCG/bLH chimera, D10 - *Homo sapiens*, 145 aa.

Plus Strand HSPs:

Score = 188 (66.2 bits), Expect = 5.0e-14, P = 5.0e-14
Identities = 40/101 (39%), Positives = 58/101 (57%), Frame = +1

Query: 76 SSGNLRTFVGCAVREFTFLAKKPGCRG-LRITTDACWGRCEWKE--PILEPPYIEAHR 246
S G LR C T A+K C + TT C G C + ++ P++ PP + R
Sbjct: 1 SRGPLRPL--CQPINATLAAEKEACPVCITFTTSICAGYCPSMKRVLPVILPPMPQ---R 55

Query: 247 VCTYNETKQVTVKLPNCAPGVDPFYTYTPVAIRCDGACSTATTE 378
VCTY+E + +V+LP C PGVDP ++PVA+ C CG C ++T+
Sbjct: 56 VCTYHELRFASVRLPGCPPGVDPMVSPVALSCHCGPCRLSSTD 99

>patp:W65110 Equine chorionic gonadotropin beta-chain protein - *Equus caballus*, 169 aa.

Plus Strand HSPs:

Score = 175 (61.6 bits), Expect = 1.2e-12, P = 1.2e-12
Identities = 43/116 (37%), Positives = 60/116 (51%), Frame = +1

Query: 31 MALLLLAGYGCVLGASSGNLRTFVGCAVREFTFLAKKPGCR-GLRITTDACWGRCEWKE 207
+ L +L G V AS G LR C T A+K C + TT C G C + +
Sbjct: 7 LLLWMLLSVGGVW-ASRGPLRPL--CRPINATLAAEKEACPICITFTTSICAGYCPSMVR 63

Query: 208 PILEPPYIEAHR-VCTYNETKQVTVKLPNCAPGVDPFYTYTPVAIRCDGACSTATTE 378
+ P + A + VCTY E + +++LP C PGVDP ++PVA+ C CG C TT+
Sbjct: 64 VM--PAALPAIPQPVCTYRELRFASIRLPGCCPPGVDPMVSPVALSCHCGPCQIKTTD 119

ClustalW alignment for NOVGN:

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (i.e., regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (e.g. L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

GTHB_CYPCA	GTHB_CYPCA
Q98349_GTHB2_GOLDFISH	Q98349_GTHB2_GOLDFISH
LSHB_BOVIN	LSHB_BOVIN
LSHB_SHEEP	LSHB_SHEEP
novel_gonadotropin	novel_gonadotropin
GTHB_CYPCA	GTHB_CYPCA
Q98349_GTHB2_GOLDFISH	Q98349_GTHB2_GOLDFISH
LSHB_BOVIN	LSHB_BOVIN
LSHB_SHEEP	LSHB_SHEEP
novel_gonadotropin	novel_gonadotropin
GTHB_CYPCA	GTHB_CYPCA
Q98349_GTHB2_GOLDFISH	Q98349_GTHB2_GOLDFISH
LSHB_BOVIN	LSHB_BOVIN
LSHB_SHEEP	LSHB_SHEEP
novel_gonadotropin	novel_gonadotropin

Figure 9A

NOVINTRA A cDNA sequence:

Regions 116708 to 116812 (1-105bp), 117121 to 117248 (106-233p), and 117529 to 117778 (234-483bp).

CACTGTCATACTGTTTCAGAATTAAATATGCAGACCAGAAGGCTCTATACACAAGAG
ATGGCCAGCTGCTGGTGGGAGATCCTGTTGCAGACAACCTGCTGTGCAGAGAAGATC
TGCATACTTCCTAACAGAGGCTTGGCCCGCACCAAGGTCCCCATTTTCCTGGGGATC
CAGGGAGGGAGCCGCTGCCTGGCATGTGTGGAGACAGAAGAGGGGCCTTCCCTACA
GCTGGAGCCATCCACCTTGCCCCCACAGGATGTGAACATTGAGGAACTGTACAAAG
GTGGTGAAGAGGCCACACGCTTCACCTTCTTCCAGAGCAGCTCAGGCTCCGCCTTCA
GGCTTGAGGCTGCTGCCTGGCCTGGCTGGTTCCTGTGTGGCCCGGCAGAGCCCCAGC
AGCCAGTACAGCTCACCAAGGAGAGTGAGCCCTCAGCCCGTACCAAGTTTTACTTTG
AACAGAGCTGGTAGGGAGACAGGAACTGC

Figure 9B

NOVINTRA A Protein sequence:

LSYCFRIKYADQKALYTRDGQLLVGDPVADNCCAEEKICILPNRGLARTKVPIFLGIQGG
RCLACVETEEGPSLQLEPSTLPPQDVNIEELYKGGEEATRFTFFQSSSGSAFRLEAAAWP
GWFLCGPAEPQQPVQLTKESEPSARTKFYFEQSW

Figure 10A

BlastN for NOVINTRA A:

gb:GENBANK-ID:AF072476|acc:AF072476 Equus caballus interleukin-1 receptor
antagonist secretory form (IL-1ra) gene, partial cds - Equus caballus,
221

bp

Top Previous Match Next Match

Length = 221

Plus Strand HSPs:

Score = 321 (48.2 bits), Expect = 8.1e-08, P = 8.1e-08

Identities = 147/218 (67%), Positives = 147/218 (67%), Strand = Plus / Plus

Query: 253 AGGATGTGAACATTGAGGAAGTACAA-AGGTGGTGAAGAGGCCACACGCTTCACCTTC 311

AGG GT AACAT GA CTG CAA A G GA GAG CA CGCTTCACCTTC

Sbjct: 4 AGGCAGTTAACATCACTGACCTGAGCAAGAACAAG-GAGGAGAACAAGCGCTTCACCTTC 62

Query: 312 TTCCAGAGCAG-CTCAGGCTCCGCCTTCAGGCTT-GAGGCTGCTGCCCTGGCCTGGCTGGT 369

TCC G CA C GGC CC CC CAG CTT GAG CTGC GCCTG CCTGGCTGGT

Sbjct: 63 ATCC-GCTCAAACAGTGGCCCCACCAACAG-CTTCGAGTCTGCCGCCTGCCCTGGCTGGT 120

Query: 370 TCCTGTGTGGCCCGGCAG-AGCCCCAGCAGCCAGTACAGC-TCACCAAGGAG---AGTGA 424

TCCT TG CG CAG AG C A C GCC GT CAGC TCACCAA AG A GA

Sbjct: 121 TCCTCTGCACGGCG-CAGGAGGCAGACCGGCCCGT-CAGCCTCACCAACAAGCCCCAAAGA 178

Query: 425 GCCCT-CAGCCCGT-ACCAAGTTTACTTTGAACAGAGCTGGTAG 467

G CCT CA GT ACCAAGTT TACTT A AG C GTAG

Sbjct: 179 GTCTTTCATG--GTCACCAAGTTCTACTTCCAGGAGGACCAGTAG 221

Figure 10B

BlastX for NOVINTRA A:

ptnr:TREMBLNEW-ACC:CAB59831 IL-1L1 PROTEIN - Mus musculus (Mouse), 155 aa.
Top Previous Match Next Match
Length = 155

Plus Strand HSPs:

Score = 309 (108.8 bits), Expect = 8.0e-27, P = 8.0e-27
Identities = 70/149 (46%), Positives = 93/149 (62%), Frame = +3

```
Query: 12 CFRIKYADQKALYTRDGQLLVGDPVADNCC-AEKICILPNRGLARTKVPIFLGIQGGSRC 188
      CFR+K + K LY + QLL G A+ E+I ++PNR L + P+ LG+QGG+C
Sbjct: 8 CFRMKDSALKVLYLHNNQLLAGGLHA EKVIKGEEISVVPNRALDASLSPVILGVQGGSC 67

Query: 189 LACVETEEGPSLQLEPSTLPPQDVNIEELYKGGEATRFTFFQSSSGSAFRLEAAAWPGW 368
      L+C TE+GP L+LEP VNI ELY G +E+ FTF++ G E+AA+PGW
Sbjct: 68 LSC-GTEKGPIKLKLEP-----VNIMELYLGAKESKSFTFYRRDMGLTSSFESAAYPGW 119

Query: 369 FLCGPAEPQQPVQLTKESEPSAR----TKFYFEQ 458
      FLC E QPV+LT+ E A T FYF+Q
Sbjct: 120 FLCTSPEADQPVRLTQIPEDPAWDAPITDFYFQQ 153
```

>ptnr:SPTREMBL-ACC:Q9UBH0 FIL1 DELTA (INTERLEUKIN-1 LIKE PROTEIN 1)
(INTERLEUKIN-1 RECEPTOR ANTAGONIST HOMOLOG 1) (INTERLEUKIN-1 DELTA) - Homo
sapiens (Human), 155 aa.

Plus Strand HSPs:

Score = 285 (100.3 bits), Expect = 4.3e-24, P = 4.3e-24
Identities = 67/149 (44%), Positives = 89/149 (59%), Frame = +3

```
Query: 12 CFRIKYADQKALYTRDGQLLVGDPVADNCC-AEKICILPNRGLARTKVPIFLGIQGGSRC 188
      CFR+K + K LY + QLL G A E+I ++PNR L + P+ LG+QGG+C
Sbjct: 8 CFRMKDSALKVLYLHNNQLLAGGLHAGKVIKGEEISVVPNRWLDASLSPVILGVQGGSC 67

Query: 189 LACVETEEGPSLQLEPSTLPPQDVNIEELYKGGEATRFTFFQSSSGSAFRLEAAAWPGW 368
      L+C +E P+L LEP VNI ELY G +E+ FTF++ G E+AA+PGW
Sbjct: 68 LSCGVGQE-PTLTLEP-----VNIMELYLGAKESKSFTFYRRDMGLTSSFESAAYPGW 119

Query: 369 FLCGPAEPQQPVQLTKESEPSAR----TKFYFEQ 458
      FLC E QPV+LT+ E T FYF+Q
Sbjct: 120 FLCTVPEADQPVRLTQLPENGWGNAPITDFYFQQ 153
```

Figure 11

ClustalW for NOVINTRA A:

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (i.e., regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (e.g. L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

Sequences used:

- 1) X86458spoil1 (cDNA encoding a human spoil-I protein); X86459spoil2 (cDNA encoding a human spoil-II protein); X89432-il1delta (human IL-1 delta encoding cDNA); Q14628 (intracellular IL-1 receptor antagonist type II-human); G512010il1beta (ovine IL-1 beta - pig)

```

X86458spoil1  - - - - - DNHTMRGTPGDA - - - - - DGG - - GRAVYQS - - - - -
X86459spoil2  - - - - - DNHTMRGTPGDA - - - - - DGG - - GRAVYQSSESNAVGMGLWRLRPSALTLSPV
X89432-il1delta - - - - - MALADLYEEG - - - - - GGG - - GGEDNADSK - - - - - E - - - - -
Q14628        - - - - - MALADLYEEG - - - - - GGG - - GGEDNADSK - - - - - E - - - - -
il1beta-1DNA  - - - - - MALADLYEEG - - - - - GGG - - GGEDNADSK - - - - - E - - - - -
G512010il1beta MATVPEPINEVMAYYSDENELLFEVDGPKQMKSCQHLDLGSMGDGNIQLQISHQLYNKS

X86458spoil1  - - - - - MCKPITGTINDLNQQVWTLQGQNLVAVPRSDS - - VTPVTVAVIT
X86459spoil2  EAPAFSAPLECTLPFPVCKPITGTINDLNQQVWTLQGQNLVAVPRSDS - - VTPVTVAVIT
X89432-il1delta - - - - - MVLSGALCFRMDKSAKVLVYLHNNQLLAGGLHA - - - - - CKVIKGEEL
Q14628        - - - - - TICRPSGRKSSKMQAFRIWDVNQKTFYLRNNQLVAGYLQG - - - - - PNVNCEEKI
il1beta-1DNA  - - - - - GPSALSYCFRIKYADQKALYTRDGLLVGDPVA - - - - - DNCCAELKI
G512010il1beta FRQVVSIVAMEKLRSRAYEHVFRDDDLRSILSEIFEEEPVIFETSSDELECDAAVQSVK

X86458spoil1  CKYPEAL - - - - - EQGRGDPIYLGIONPEM
X86459spoil2  CKYPEAL - - - - - EQGRGDPIYLGIONPEM
X89432-il1delta SVVPNRW - - - - - LDASLSPVILGVQGGSQ
Q14628        DVVP - - - - - IEPHALLGIHGGKM
il1beta-1DNA  CILPNRG - - - - - LARTKVPILGIQGGSR
G512010il1beta CKLQDR EQKSLVLDSPCVLKALHLLSQEMSREVVFCMSFVQGEERDNKIPVALGIRDKNL

X86458spoil1  CLYCEKVGEQPTLQLKE - - - - - QKIMDLYGQPEPVKPFLLFYRAKTGRTSTLESVAFPD
X86459spoil2  CLYCEKVGEQPTLQLKE - - - - - QKIMDLYGQPEPVKPFLLFYRAKTGRTSTLESVAFPD
X89432-il1delta CLSCG-VGQEP TLTLEP - - - - - VNIMELYLGAKESKSFTFYRRDMGLTSSFESAAYPG
Q14628        CLSCVKSGDETRLQLEA - - - - - VNI TDLS ENRKQDKRFAFIRSDSGPTTSFESAACPG
il1beta-1DNA  CLACVETE EGPSLQLEPSTLPPQDVNI EELYKGGEEATRFTTFQSSSGSAFRLEAAAWPG
G512010il1beta YLSCVKK GDTPTLQLEE - - - - - VDPKVYPKRNMKRFVFKTEIKNTVEFESVLYPN

X86458spoil1  WFIASS - KR DQPIILTS ELGKS - - - - - YNTAFELNIND -
X86459spoil2  WFIASS - KR DQPIILTS ELGKS - - - - - YNTAFELNIND -
X89432-il1delta WFLCTVPEADQPVRLTQLPENGGWNAPI TDFYFQQCD -
Q14628        WFLCTAMEADQPVSLTNMPDEG - - - - - VMVTKFYFQED -
il1beta-1DNA  WFLCGPAEPQPPVQLTKES EPS - - - - - ARTKFFFEQSW -
G512010il1beta WYISTSQIEEKPVFLGRFRGGQ - - - - - DITDFRMETLSP

```

Figure 12A

NOVINTRA B cDNA sequence:

Regions 116968 to 117028 (1-61bp), 104067 to 104164 (62-159bp), 101958 to 102098 (160-300bp), and 100915 to 101134 (301-520bp) of genomic clone (-frame).

ATGGGCACACCTGGCCTGGCCCTGCATGCAGACTGGACGGTGAGCCAGGACTTCTG
CAGGACACCCAAATCCTATGCTATTCGTGATTCTCGACAGATGGTGTGGGTCCTGAG
TGGAAATTCTTTAATAGCAGCTCCTCTTAGCCGCAGCATTAAGCCTGTCACTCTTCAT
TTAATAGCCTGTAGAGACACAGAATTCAGTGACAAGGAAAAGGGTAATATGGTTTA
CCTGGGAATCAAGGGAAAAGATCTCTGTCTCTTCTGTGCAGAAATTCAGGGCAAGCC
TACTTTGCAGCTTAAGGAAAAAATATCATGGACCTGTATGTGGAGAAGAAAGCAC
AGAAGCCCTTTCTCTTTTCCACAATAAAGAAGGCTCCACTTCTGTCTTTCAGTCAGT
CTCTTACCCTGGCTGGTTCATAGCCACCTCCACCACATCAGGACAGCCCATCTTTCTC
ACCAAGGAGAGAGGCATAACTAATAACACTAACTTCTACTTAGATTCTGTGGAATA
AATCCAGC

Figure 12B

NOVINTRA B Protein sequence:

MGTPGLALHADWTVSQDFCRTPKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLI
ACRDTEFSDKEKGNMVYLGKGDLCFCAEIQ GKPTLQLKEKNIMDL YVEKKAQKPF
FFHNKEGSTSVFQSVSPGWFIATSTTSGQPIFLTKERGITNNTNFYLDSE

Figure 13A

BlastN for NOVINTRA B:

gb:GENBANK-ID:PIGIRAP|acc:L38849 Sus scrofa (clone p0328w) IRAP1 mRNA,
complete cds - Sus scrofa, 563 bp (RNA).

Top Previous Match Next Match

Length = 563

Plus Strand HSPs:

Score = 309 (46.4 bits), Expect = 1.1e-07, P = 1.1e-07

Identities = 197/331 (59%), Positives = 197/331 (59%), Strand = Plus / Plus

Query: 169 CATTTAATAGCCTGTA-GAGAC-ACAGAATTCAGTGACAAGGAAAAGGCTAATATGGTTT 226
CA TA TA CTG A GAGA A AGA T GTG C G AG T AT T GT T
Sbjct: 217 CAAATACTAAACTGGAAGAGAAGATAGATGTG-GTGCCT--GTTGAGCCTCATTTTGTGT 273

Query: 227 ACCTGGGAATCAAGGGAAAAGATCTCTGTCTCTTCTGTGCAGAAATTCAGGGCAAGCC-T 285
CCTGGG ATC A GGA A CT TG CT T CTGTG AA T C GG A G T
Sbjct: 274 TCCTGGGGATCCATGGAGGGAAGCTGTGCCTGTCTCTGTGTC-AAGT-CTGGTGATGAGAT 331

Query: 286 -ACTTTGCAGCTTAAGGAAAAAATATCATGGACCTGTATGTGGAGAAGAAAGCAC-AGA 343
A T CAG T A G A AA ATCA GACCTG A GA AG AGCA A A
Sbjct: 332 GAAGCTCCAGTTGGACGCAGTTAACATCACAGACCTG-AGAAAGAACAGCGAGCAGGACA 390

Query: 344 AGCCCTTTCTCTTTTCCACAATAA-AGAAGGCTCCACTTCTGTCTTTTCTCAGTCAGTCTCT 402
AGC CTT CTT TCC C A AG GGC CCAC C CTTT AGTCAG C C
Sbjct: 391 AGCGCTTCACCTTCATCCGCTCCGACAGT-GGCCCCACACCAGCTTTGAGTCAGCCGCC 449

Query: 403 TACCCTGGCTGGTTTATAGCCACCTCCACCACAT-CAGGACAGCCCATCTTTCTCACCAA 461
T CCTGGCTGGTTC T CAC T CAC A A CAG CAGCC T CTCACCAA
Sbjct: 450 TGTCTGGCTGGTTCCTCTGCAC-TGCACTAGAGGCAGACCAGCCTGTTGGCCTCACCAA 508

Query: 462 GGAGAG-AG-GCATAACT-AATAACACTAACTTCTACTT 497
G A GCA T AA CAC AA TTCTACTT
Sbjct: 509 CACGCCCAAAGCAGCCGTCAAGGTCACCAAGTTCTACTT 547

Figure 13B

BlastX for NOVINTRA B:

>ptnr:SPTREMBL-ACC:Q9UHA5 FIL1 ETA - Homo sapiens (Human), 157 aa.
Plus Strand HSPs:

Score = 777 (273.5 bits), Expect = 3.2e-76, P = 3.2e-76
Identities = 149/149 (100%), Positives = 149/149 (100%), Frame = +1

Query: 64 PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTEFSDKEKGNMVYLGIGK 243
PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTEFSDKEKGNMVYLGIGK
Sbjct: 9 PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTEFSDKEKGNMVYLGIGK 68

Query: 244 KDLCLFCAEIQGKPTLQLKEKNIMDLYVEKKAQKPFLFFHNKEGSTSVFQSVSYPGWFIA 423
KDLCLFCAEIQGKPTLQLKEKNIMDLYVEKKAQKPFLFFHNKEGSTSVFQSVSYPGWFIA
Sbjct: 69 KDLCLFCAEIQGKPTLQLKEKNIMDLYVEKKAQKPFLFFHNKEGSTSVFQSVSYPGWFIA 128

Query: 424 TSTTSGQPIFLTKERGITNNTNFYLDSE 510
TSTTSGQPIFLTKERGITNNTNFYLDSE
Sbjct: 129 TSTTSGQPIFLTKERGITNNTNFYLDSE 157

>ptnr:SPTREMBL-ACC:Q9NZH7 INTERLEUKIN-1 HOMOLOG 2 - Homo sapiens (Human), 164 aa.
Plus Strand HSPs:

Score = 411 (144.7 bits), Expect = 1.9e-37, P = 1.9e-37
Identities = 80/85 (94%), Positives = 81/85 (95%), Frame = +1

Query: 64 PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTEFSDKEKGNMVYLGIGK 243
PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTEFSDKEKGNMVYLGIGK
Sbjct: 9 PKSYAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTEFSDKEKGNMVYLGIGK 68

Query: 244 KDLCLFCAEIQGKPTLQLKEKNIMD 318
KDLCLFCAEIQGKPTLQLK + D
Sbjct: 69 KDLCLFCAEIQGKPTLQLKLQGSQD 93

>ptnr:TREMBLNEW-ACC:AAF02757 INTERLEUKIN-1 RECEPTOR ANTAGONIST HOMOLOG
- Homo sapiens (Human), 155 aa.

Top Previous Match Next Match
Plus Strand HSPs:

Score = 197 (69.3 bits), Expect = 5.9e-15, P = 5.9e-15
Identities = 52/147 (35%), Positives = 76/147 (51%), Frame = +1

Query: 73 YAIRDSRQMVWVLSGNSLIAAPLSRSIKPVTLHLIACRDTEFSDKEKGNMVYLGIGKDL 252
+ ++DS V L N L+A L K + I+ + D ++ LG++G
Sbjct: 9 FRMKDSALKVLYLHNNQLLAGGLHAG-KVIKGEISVVPNRWLDASLSPVI-LGVQGSQ 66

Query: 253 CLFCAEIQGKPTLQLKEKNIMDLYVEKKAQKPFLFFHNKEGSTSVFQSVSYPGWFIATST 432
CL C Q +PTL L+ NIM+LY+ K K F F+ G TS F+S +YPGWF+ T
Sbjct: 67 CLSCGVGQ-EPTLTLEPVNIMELYLGAKESKSFTFYRRDMGLTSSSFESAAYPGWFLCTVP 125

Query: 433 TSGQPIFLTK--ERGITNN--TNFYLDSE 510
+ QP+ LT+ E G N T+FY +
Sbjct: 126 EADQPVRLTQLPENGGWNAIPITDFYFQQCD 155

Figure 14

ClustalW for NOVINTRA B:

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (*i.e.*, regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (*e.g.* L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

Sequences used:

- 2) X86459spoil2 (cDNA encoding a human spoil-II protein; Q14628 (intracellular IL-1 receptor antagonist type II-human); AAF02757 (intracellular IL-1 receptor antagonist type II-human); G512010; (OVINE IL-1 BETA - Pig)

Multiple Alignment:

```

il1beta2DNA      - - - - - M G T P G L A L H A D W T V S Q D - - - - -
X86459spoil2     - - - - - D N H T M R G T P G D A D G G G R A V Y Q S S E S N
Q14628           - - - - - M A L A D L Y E E G G G G G E G E D N A D S K E -
AAF02757         - - - - -
G512010il1beta  M A T V P E P I N E V M A Y S D E N E L L F E V D G P K Q M K S C T Q H L D L G S M E D G N I Q L Q I S H Q L Y N K S

il1beta2DNA      - - - - - F C R T - - - - - P K S Y A I R - - - - -
X86459spoil2     A V G M G L W R L R P S A L T L S P V E A P A F S A P L C T L P F P P V C K - P I T G T I N - - - - -
Q14628           - - - - - T I C R P S G R K S S K - M Q A F R I W - - - - -
AAF02757         - - - - - - M V L S G - A L C F R M K - - - - -
G512010il1beta  F R Q V V S V I V A M E K L R S R A Y E H V F R D D D L R S I L S F I F E E E P V I F E T S S D E L L C D A A V Q S V K

il1beta2DNA      - - - - - D S R Q M V W V L S G N S L I A A P L S R S I K P V T L H L I A C R D T E F S D K - E K G N M V Y L G I K K D
X86459spoil2     - - - - - D L N Q Q V W T L Q G Q N L V A V P R S D S V T P V T V A V I T C K Y P E A L E Q - G R G D P I Y L G I Q N P E
Q14628           - - - - - D V N Q K T E Y L R N N Q L V A G Y L Q - - G P N V N L E E K I D V V P - - - - - I E P H A L F L G I H C G K
AAF02757         - - - - - D S A L K V L Y L H N N Q L L A G G L H - - A G K V I K G E E I S V V P N R W L D - A S L S P V I L G V Q G G S
G512010il1beta  C K L Q D R E Q K S L V L D S - P C V L K A L H L L S Q E M S R E V V F C M S F V Q G E E R D N K I P V A L G I R D K N

il1beta2DNA      L C L F C A E I Q G K P T L Q L K E K N I M D L Y V E K K A Q K P F L F E H N K E G S T S V F Q S V S Y P G W F I A T S
X86459spoil2     M C L Y C E K V G E Q P T L Q L K E Q K I M D L Y G Q P E P V K P F L F Y R A K T G R T S T L E S V A E P D W F I A S S
Q14628           M C L S C V K S G D E T R L Q L E A V N I T D L S E N R K Q D K R F A F I R S D S G P T T S F E S A A C P G W F L C T A
AAF02757         Q C L S C G - V G Q E P T L T L E P V N I M E L Y L G A K E S K S F T F Y R R D M G L T S S F E S A A Y P G W F L C T V
G512010il1beta  L Y L S C V K K G D T P T L Q L E E V D P K V Y P - K R N M E K R F V F Y K T E I K N T V E F E S V L Y P N W Y I S T S

il1beta2DNA      T T S G Q P I F L T K E R - - G - - I T N N T N F Y L D S V E -
X86459spoil2     K R D - Q P I I L T S E L - - G - - K S Y N T A F E L N I N D -
Q14628           M E A D Q P V S L T N M P D E G - - V M V T K F Y F Q E D E -
AAF02757         P E A D Q P V R L T Q L P E N G G W N A P I T D F Y F Q Q C D -
G512010il1beta  Q I E E K P V F L G R F R - - G - - G Q D I T D F R M E T L S P

```

Figure 15A

NOVINTRA C cDNA sequence:

Region 168700 to 168880 (1-181bp), 169967 to 170118 (182-331bp) and 170635 to 170694 (332-391bp) of the genomic clone (- frame).

```
GATATCAATCATCGGGTGTGGGTTCTTCAGGACCAGACGCTCATAGCAGTCCCGAGG
AAGGTGTTCCCGAGTCACTATTGCCTTAATCTCATGCCGACATGTGGAGACCCTTGAG
AAAGACAGAGGGAACCCCATCTACCTGGGCCTGAATGGACTCAATCTCTGCCTGAT
GTGTGCTAAAGTCGGGGACCAGCCACACTGCAGCTGAAGCTTCAGGAAAAGGATA
TAATGGATTTGTACAACCAACCCGAGCCTGTGAAGTCCTTTCTCTTCTACCACAGCC
AGAGTGGCAGGAACCTCCACCTTCGAGTCTGTGGCTTCCCTGGGTGGTTCATCGCTG
TCAGCTCTGAAGGAGGCTGTCCTCTCATCCTTACCCAAGAACTGGGGAAAG
```

Figure 15B

NOVINTRA C Protein sequence:

```
DINHRVWVLQDQTLIAVPRKVPVTIALISCRHVETLEKDRGNPIYLGLNGLNLCLMCAK
VGDQPTLQLKLQEKDMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIASSEGCG
PLILTQELGK
```

Figure 16A

BlastN for NOVINTRA C:

gb:GENBANK-ID:PIGIRAP|acc:L38849 Sus scrofa (clone p0328w) IRAP1 mRNA,
complete cds - Sus scrofa, 563 bp (RNA).

Top Previous Match Next Match

Length = 563

Minus Strand HSPs:

Score = 274 (41.1 bits), Expect = 5.6e-06, P = 5.6e-06

Identities = 150/244 (61%), Positives = 150/244 (61%), Strand = Minus / Plus

Query: 258 TCTACCTGGGCCTGAATGGACTCAATCTCTGCCTGATGTGTGCTAAAGTCGGG-GACCAG 200
T T CCTGGG T ATGGA AA CT TGCCTG TGTG T AAGTC GG GA AG
Sbjct: 271 TGTTCCTGGGGATCCATGGAGGGAAGCTGTGCCTGTCCTGTG-TCAAGTCTGGTGATGAG 329

Query: 199 CCCACACTGCAGCTGAAGCTTCAGGAAAAGGATATAATGGATTTGTACAACCAACC-CGA 141
A CT CAG TG A C CAG AA AT A GA TG A AA AAC CGA
Sbjct: 330 ATGAAGCTCCAGTTGGA-CG-CAGTTAAC---ATCACAGACCTG-AGAAAGAACAGCGA 382

Query: 140 GCCTGTGAAGTCCTTTCTCTTCTACCACAGCCAGAGTGGCAGGAACTCCACCTTCGAGTC 81
GC G AAG CTT CTTC CC C C A AGTGGC A C CCA CTT GAGTC
Sbjct: 383 GCAGGACAAGCGCTTCACCTTCATCCGCTCCGACAGTGGCCCCACCACCAGCTTTGAGTC 442

Query: 80 TGTGGCTTTCCCTGGCTGGTTTCATCGCTGT-CAGCTCTGAAGG-AGGCTGTCCTCTCATC 23
G GC T CCTGGGTGGTTC TC TG C GC CT AGG AG C CCT T C
Sbjct: 443 AGCCGCTGTCTCTGGCTGGTTTCCTC--TGCACTGCACTAGAGGCAGACCAGCCTGTTGGC 500

Query: 22 CTTACCCA 15
CT ACC A
Sbjct: 501 CTCACCAA 508

Figure 16B

BlastX for NOVINTRA C:

>ptnr:SPTREMBL-ACC:Q9UHA7 FIL1 EPSILON - Homo sapiens (Human), 158 aa.
Plus Strand HSPs:

Score = 646 (227.4 bits), Expect = 2.4e-62, P = 2.4e-62
Identities = 126/130 (96%), Positives = 127/130 (97%), Frame = +1

Query: 1 DINHRVWVLQDQTLIAVPRK--VFPVTIALISCRHVETLEKDRGNPIYLGLNGLNLCCLMC 174
DINHRVWVLQDQTLIAVPRK + PVTIALISCRHVETLEKDRGNPIYLGLNGLNLCCLMC
Sbjct: 17 DINHRVWVLQDQTLIAVPRKDRMSPVTIALISCRHVETLEKDRGNPIYLGLNGLNLCCLMC 76

Query: 175 AKVGDQPTLQLKLEKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIASSEG 354
AKVGDQPTLQLK EKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIASSEG
Sbjct: 77 AKVGDQPTLQLK--EKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIASSEG 134

Query: 355 GCPLILTQELGK 390
GCPLILTQELGK
Sbjct: 135 GCPLILTQELGK 146

>ptnr:SPTREMBL-ACC:Q9NZH8 INTERLEUKIN-1 HOMOLOG 1 - Homo sapiens, 169 aa.

Plus Strand HSPs:

Score = 416 (146.4 bits), Expect = 5.7e-38, P = 5.7e-38
Identities = 82/130 (63%), Positives = 101/130 (77%), Frame = +1

Query: 1 DINHRVWVLQDQTLIAVPRK--VFPVTIALISCRHVETLEKDRGNPIYLGLNGLNLCCLMC 174
D+N +VW LQ Q L+AVPR V PVT+A+I+C++ E LE+ RG+PIYLG+ +CL C
Sbjct: 29 DLNQQVWTLQGGQNLVAVPRSDSVTPVTVAVITCKYPEALEQGRGDPIYLGIONPEMCLYC 88

Query: 175 AKVGDQPTLQLKLEKDIMDLYNQPEPVKSFLFYHSQSGRNSTFESVAFPGWFIASSEG 354
KVG+QPTLQLK E+ IMDLY QPEPVK FLFY +++GR ST ESVAFP WFIA SS+
Sbjct: 89 EKVGEQPTLQLK--EQKIMDLYGQPEPVKPFIFYRAKTGRTSTLESVAFPDWFIA-SSKR 145

Query: 355 GCPLILTQELGK 390
P+ILT ELGK
Sbjct: 146 DQPIILTSELGK 157

>ptnr:SWISSPROT-ACC:P25085 INTERLEUKIN-1 RECEPTOR ANTAGONIST PROTEIN
PRECURSOR (IL-1RA) (IL-1RN) (IRAP) - Mus musculus (Mouse), 178 aa.

Top Previous Match Next Match

Minus Strand HSPs:

Score = 173 (60.9 bits), Expect = 2.1e-12, P = 2.1e-12
Identities = 35/81 (43%), Positives = 50/81 (61%), Frame = -1

Query: 259 IYLGLNGLNLCCLMCAKVGDQPTLQLKLEKDIMDLYNQPEPVKSFLFYHSQSGRNSTFES 80
++LG++G LCL CAK GD ++L+L+E +I DL E K F F S+ G ++FES
Sbjct: 82 VFLGIHGGKLCCLSCAKSGDD--IKLQLEEVNITDLNKNKEEDKRFTFIRSEKGPPTSFS 139

Query: 79 VAFPGWFIASSEGCGPLILT 17
A PGWF+ + E P+ LT
Sbjct: 140 AACPGWFLCTTLEADRPVSLT 160

Figure 17

ClustalW for NOVINTRA C:

Based on this alignment, black outlined amino acid residues indicate regions of conserved sequence (i.e., regions that may be required to preserve structural or functional properties); greyed amino acid residues can be mutated to a residue with comparable steric and/or chemical properties without altering protein structure or function (e.g. L to V, I, or M); non-highlighted amino acid residues can potentially be mutated to a much broader extent without altering structure or function.

Sequences used:

- 1) IL1X_MOUSE: Locus - IL1X_MOUSE; Accession - P25085; PID - g124313
- 2) IL1X_HORSE: Locus - IL1X_HORSE; Accession - O18999; PID - g6166230
- 3) AAF02757_HUMAN: Locus - AF186094_1; Accession - AAF02757; PID - g6049805

```

IL1X_MOUSE      MEICWGPYSHLISLLILLFHSEAACRPSGKRPCCKMQAFRIWDINQKTFYLRNNQLIAGY
IL1X_HORSE      MEIRRRSVRHLIS-LLLFIFYSETACHPLGKRPCCKMQAFRIWDVNNQKTFYMRNNQLVAGY
AAF02757_Human  -----MVLSGALC-----FRMKDSALKVLYLHNNQLLAGG
Novel_IL1       -----DINHRVWVLQDQTLIAPV

IL1X_MOUSE      LGGPNIKLE---EKIDMVP-----IDLHSVFLGIHGGKLCLSCAKSGDDIKLQLEEVN-
IL1X_HORSE      LQESNTKLO---EKIDVVP-----IEPDALFLGLHGRKLCLACVKSQDEIRFQLEAVN-
AAF02757_Human  LHAGKVIKG---EEISVVPNRWLDASLSPVILGVQGGSCQLSCG-VGQEP TLTLEPVN-
Novel_IL1       RKVFPVTIALISCRHVETLEK---DRGNPIYLG L NGLNLCLMCAKVGDOPTLQLKLQEK

IL1X_MOUSE      -ITDLSKNKEEDKRFTFI RSEKGP TTSFESAACPGWFLCTTL EADRPVS LTNTPEE---P
IL1X_HORSE      -ITDLSKNKEENKRFTFI RSNSGP TTSFESAACPGWFLCTAQ EADRPVS LTNKPKE---S
AAF02757_Human  -IMELYLGAKESKSFTFYRRDMGLTSSSFESAAPGWFLCTVPEADQPVRLTQLPENGGWN
Novel_IL1       DIMDLYNQPEPVKSFLFYHSQS GRNSTFESVAFPGWFIAVSS EGGCP LI LTQELGK---

IL1X_MOUSE      LITVKFYFQEDQ
IL1X_HORSE      FMVTKFYLQEDQ
AAF02757_Human  APITDFYFQQCD
Novel_IL1       -----

```

Figure 18

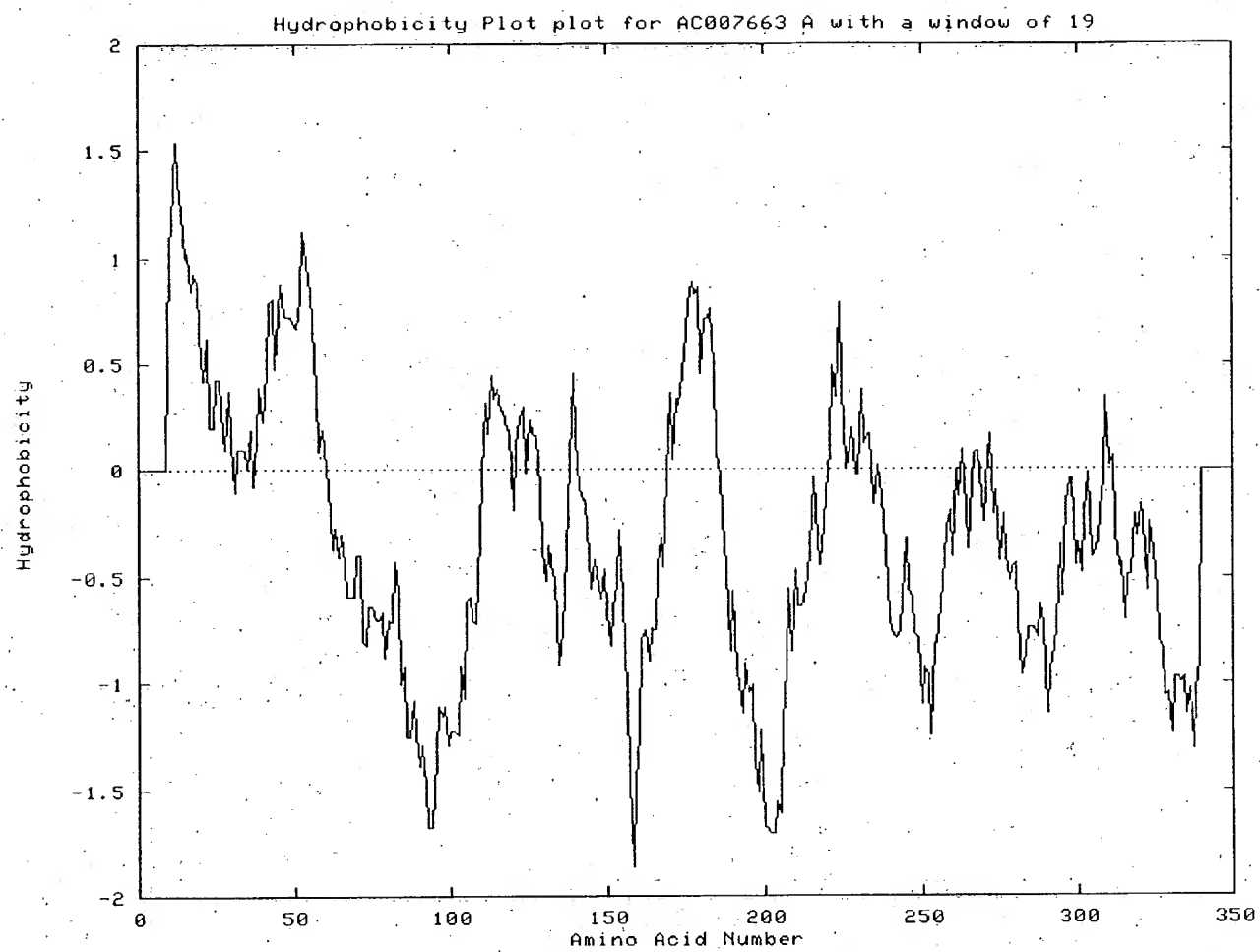


Figure 19

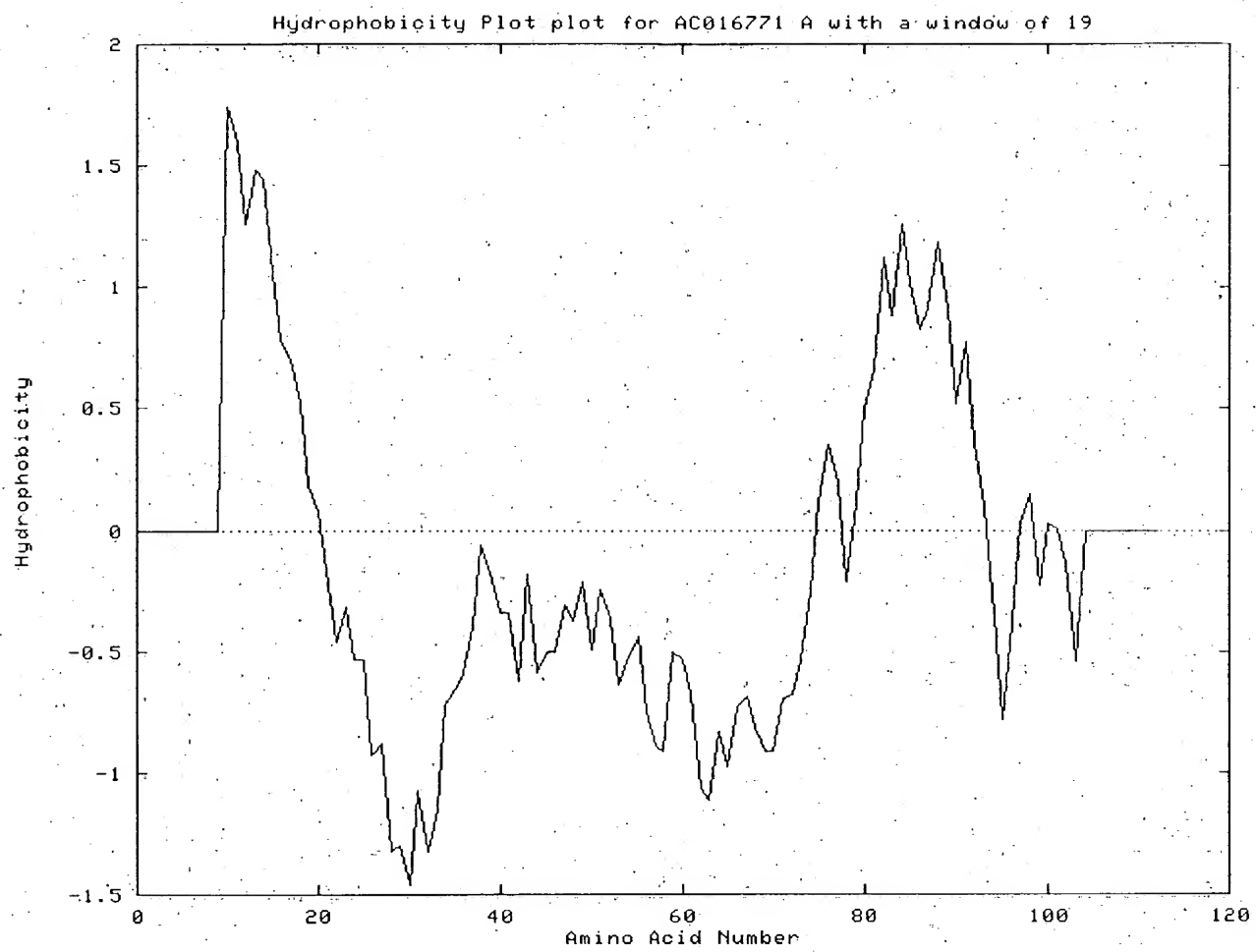


Figure 20

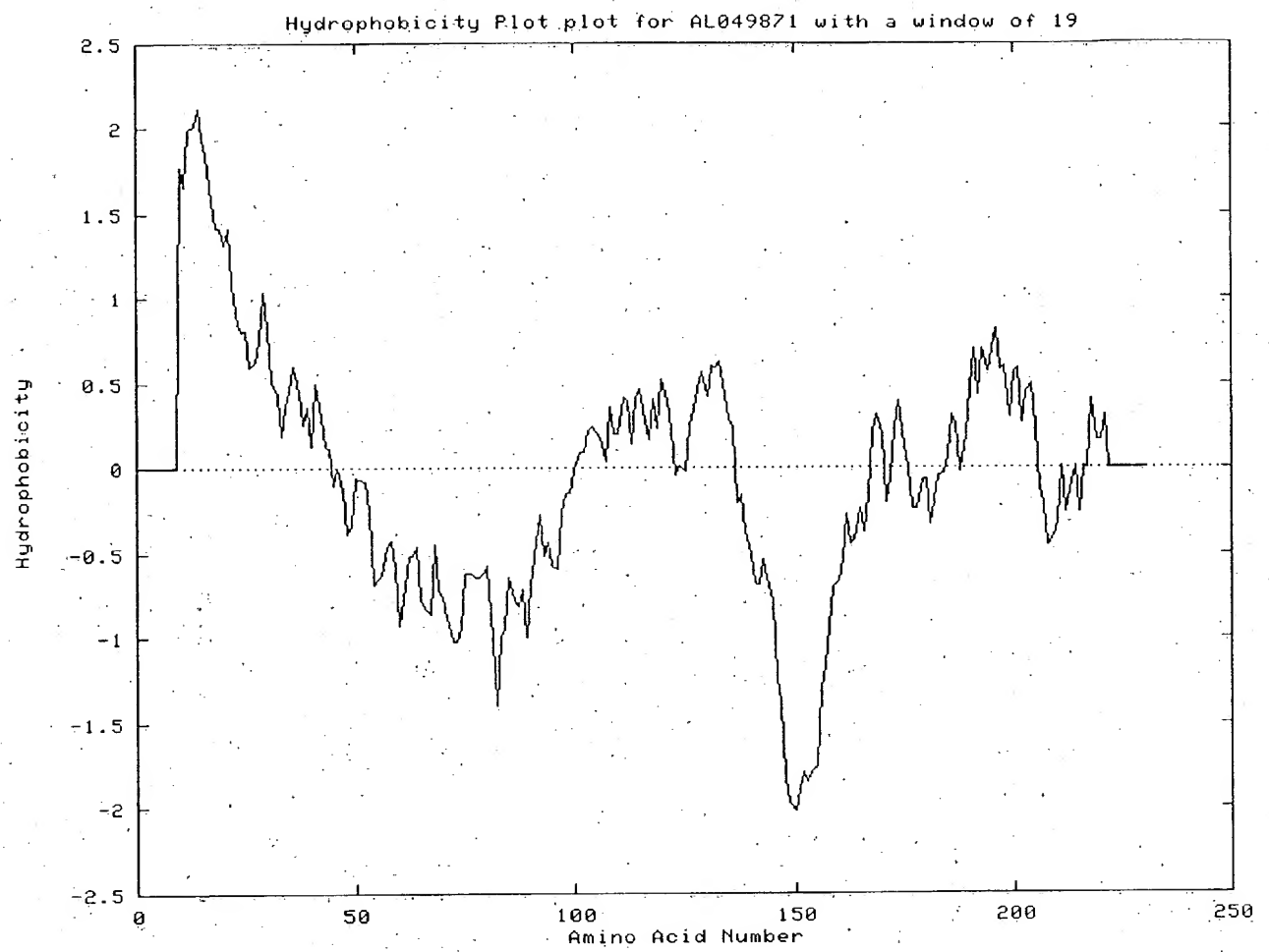


Figure 21

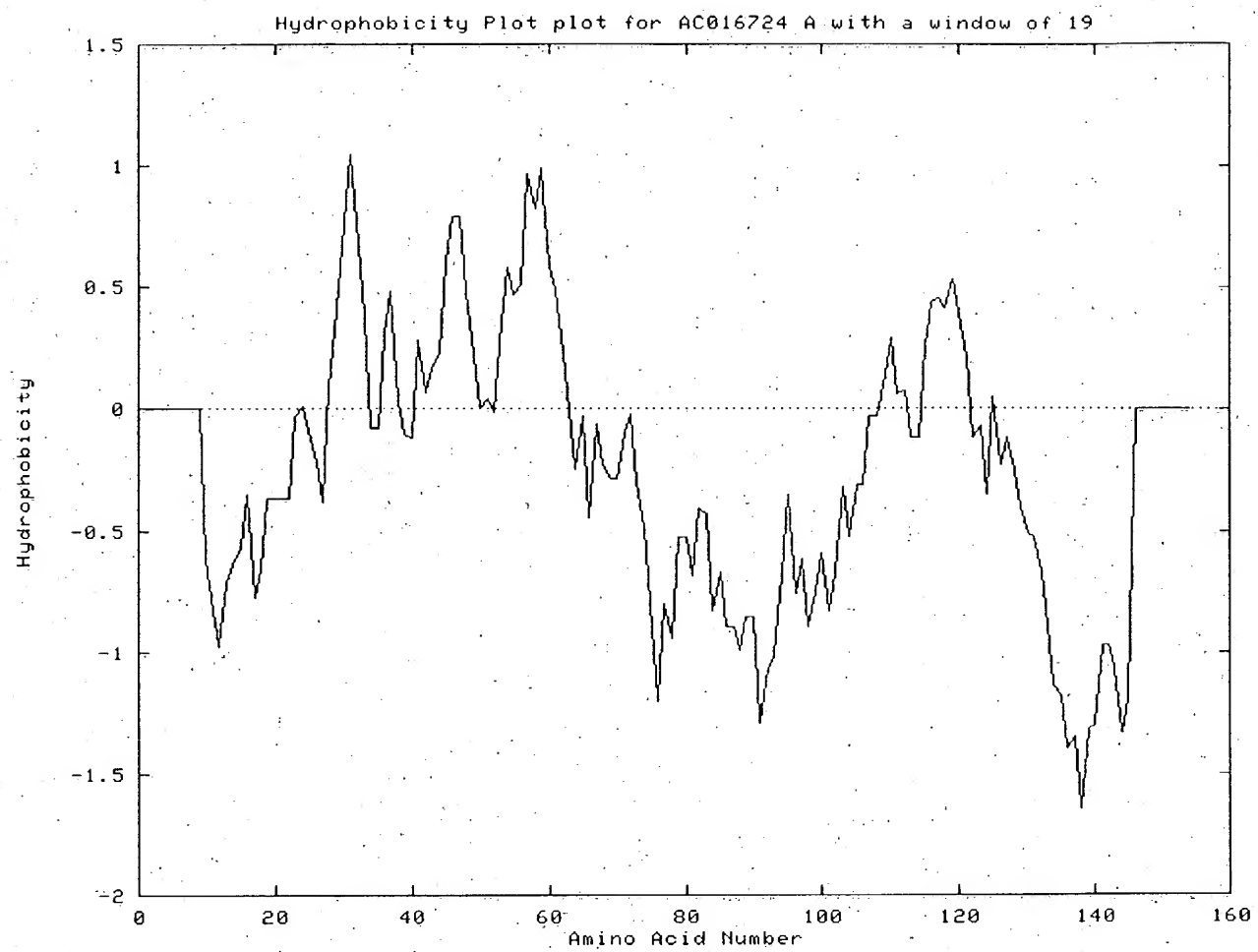


Figure 22

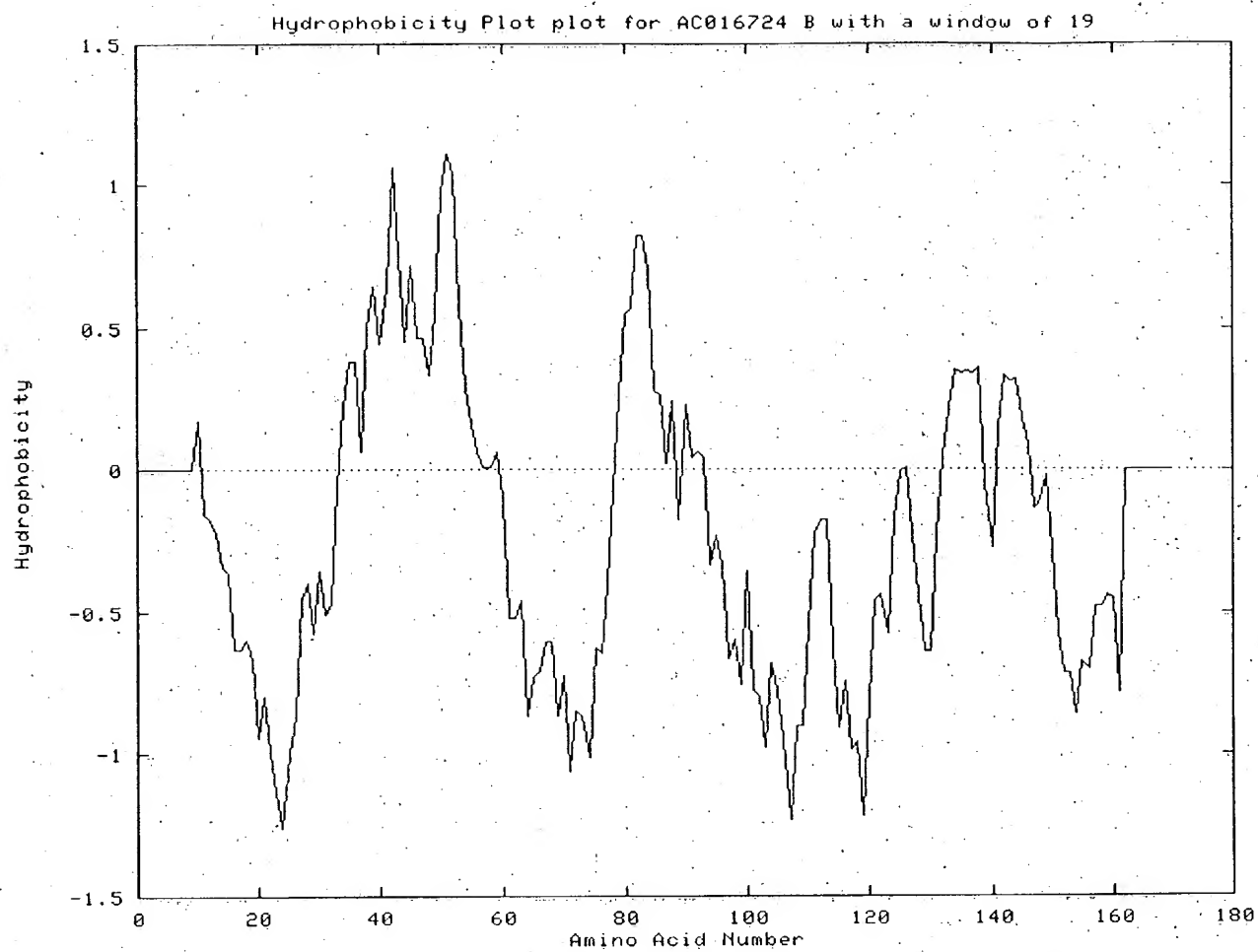


Figure 23

